

IN THE CLAIMS:

Please amend the claims as follows:

1. (Withdrawn) A method for diagnosing cancer by measuring DNA-dependent protein kinase activity in cells derived from a test subject.
2. (Withdrawn) A method for diagnosing cancer, the method comprising the steps of:
 - measuring DNA-dependent protein kinase activity in cells derived from a test subject;
 - measuring DNA-dependent protein kinase activity in cells derived from a healthy subject; and
 - comparing the DNA-dependent protein kinase activity in cells derived from the test subject and the DNA-dependent protein kinase activity in cells derived from the healthy subject.
3. (Withdrawn) The method for diagnosing cancer according to claim 1 or 2, wherein the cells are lymphoid cells.
4. (Withdrawn) A cancer diagnosis kit for diagnosing cancer by the method for diagnosing cancer according to any one of claims 1 to 3.

5. (Withdrawn) The cancer diagnosis kit for diagnosing cancer by the method for diagnosing cancer according to any one of claims 1 to 3, the kit comprising a peptide substrate which is phosphorylated by DNA-dependent protein kinase.
6. (Currently amended) A method for determining cancer susceptibility by measuring DNA-dependent protein kinase activity in cells derived from a test subject, wherein the cancer is selected from the group consisting of breast cancer, uterine cancer, and head and neck cancer.
7. (Currently amended) A method for determining cancer susceptibility, the method comprising the steps of:
 - measuring DNA-dependent protein kinase activity in cells derived from a test subject;
 - measuring DNA-dependent protein kinase activity in cells derived from a healthy subject; and
 - comparing the DNA-dependent protein kinase activity in cells derived from the test subject and the DNA-dependent protein kinase activity in cells derived from the healthy subject,wherein the cancer is selected from the group consisting of breast cancer, uterine cancer, and head and neck cancer.
8. (Original) The method for determining cancer susceptibility according to claim 6 or 7, wherein the cells are lymphoid cells.

9. (Withdrawn) A cancer susceptibility determination kit for determining cancer susceptibility by the method for determining cancer susceptibility according to any one of claims 6 to 8.
10. (Withdrawn) The cancer susceptibility determination kit for diagnosing cancer by the method for diagnosing cancer susceptibility according to any one of claims 6 to 9, the kit comprising a peptide substrate which is phosphorylated by DNA-dependent protein kinase.

Please add the following new claim:

11. (New) A method for determining cancer susceptibility, comprising: measuring DNA-dependent protein kinase activity in cells derived from a test subject; and determining cancer susceptibility based upon the measured DNA-dependent protein kinase activity, wherein the cancer is selected from the group consisting of breast cancer, uterine cancer, and head and neck cancer.

Status Summary

Claims 1-10 are pending in the present application and have been examined by the U.S. Patent and Trademark Office (hereinafter "the Patent Office"). Claims 1-5, 9 and 10 have previously been withdrawn in response to a restriction requirement. Claims 6-8 presently stand rejected.

The specification has been objected to for failing to include trademark symbols where appropriate.

Claims 6-8 have been rejected under 35 U.S.C. § 112, first paragraph, upon the contention that the specification, while enabling for determining the susceptibility of some cancers, does not reasonably provide enablement for determining cancer susceptibility in any cancer.

Claims 6 and 8 stand rejected under 35 U.S.C. § 102(b) upon the contention that the claims are anticipated by European Patent No. EP 1,184,665 to Ogawa et al. (hereinafter "Ogawa et al.").

Additionally, claims 6-8 stand rejected under 35 U.S.C. § 102(b) upon the contention that the claims are anticipated by Auckley et al. (*Carcinogenesis*, 2001, Vol. 22(5), pages 723-727; hereinafter "Auckley et al.").

By this Amendment, claims 6 and 7 have been amended and claim 11 has been added. No new matter has been added. Therefore, upon entry of the Amendment, claims 6-8 and 11 will be pending in the subject application.

Response to the Objection for Failing to Include Trademark Symbols

The specification has been objected to for failing to include trademark symbols. Specifically, the Examiner contends that the uses of the trademark "Lymphoprep" as recited in the specification do not include trademark symbols.

Applicants respectfully submit that the instances of the trademark Lymphoprep™, as found at page 9, line 12 and page 19, line 17, of the specification, have been amended to include appropriate trademark symbols. Accordingly, applicants respectfully submit that this matter has been addressed and respectfully request withdrawal of the objection.

Response to the Rejection of Claims Under 35 U.S.C. § 112, first paragraph

Claims 6-8 have been rejected under 35 U.S.C. § 112, first paragraph, upon the contention that the specification, while enabling for detecting or diagnosing cancer in cervical, uterine, lung, and breast cancer, does not reasonably provide enablement for determining cancer susceptibility in any cancer. The Examiner contends that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. Specifically, the Examiner contends that there is insufficient evidence or nexus that would lead the skilled artisan to predict the ability to determine susceptibility to just any cancer by measuring DNA-dependent protein kinase activity. Further, in view of the lack of predictability of the art to which the invention pertains, the Examiner contends that the lack of established guidelines for determining cancer susceptibility and measuring DNA-dependent protein kinase

Application Serial No.: 10/559,311

activity in any cancer type, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success.

The positions of the Examiner as summarized above with respect to the rejected claims are respectfully traversed as described below.

Applicants respectfully submit that the Patent Office has identified no sound scientific basis for the assertion that the specification does not reasonably provide enablement for determining cancer susceptibility in any cancer. According to *In re Marzocchi*, 439 F.2d 220, 169 USPQ 367 (CCPA 1971):

As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

In re Marzocchi at page 223 (emphasis added).

Furthermore, according to the Training Materials for Examining Patent Applications with Respect to 35 U.S.C. Section 112, First Paragraph-Enablement Chemical/Biotechnical Applications “the case law makes clear that properly reasoned and supported statements explaining any failure to comply with Section 112 are a requirement to support a rejection”. Citing *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Applicants respectfully submit that no such “properly reasoned and supported statements” have been presented, other than general assertions. As a result, applicants respectfully submit that the Patent Office

Application Serial No.: 10/559,311

has not satisfied its burden concerning the establishment of a *prima facie* case of lack of enablement of claims 6-8.

However, assuming *arguendo* that the Patent Office has established a *prima facie* case of lack of enablement of claims 6-8, applicants respectfully submit that claims 6 and 7 have been amended to clarify the claimed subject matter. Specifically, claims 6 and 7 have been amended to recite “wherein the cancer is selected from the group consisting of breast cancer, uterine cancer, and head and neck cancer”. Support for the amendments can be found throughout the specification, including particularly in the specification as originally filed at page 12, lines 11-15; page 19, lines 7-10; and page 24, lines 1-2. Thus, no new matter has been added by the amendments to claims 6 and 7.

Applicants respectfully disagree with the Examiner's contention that the specification does not provide any direction or guidance to assist one skilled in the art in the determination of susceptibility to cancer. Applicants direct the Examiner to Figure 1. Figure 1 is a graph showing the relationship between DNA-dependent protein kinase activity and chromosome abnormality, wherein chromosome abnormality decreases with an increase in DNA-dependent protein kinase activity and, conversely, chromosome abnormality increases with a decrease in DNA-dependent protein kinase activity. Stated another way, chromosome abnormalities are inversely related to DNA-dependent protein kinase activity. As would be appreciated by one of skill in the art, chromosome abnormalities are the result of damages to DNA molecules that result in genetic mutations. Accordingly, the accumulation of genetic mutations can lead to malignant transformations in cells,

Application Serial No.: 10/559,311

resulting in cancer. See, for example, page 7, lines 8-17 of the specification. Further, DNA-dependent protein kinase plays a role in preventing genetic mutations and chromosome abnormalities. See, for example, page 3, lines 6-13. Therefore, a decrease in DNA-dependent protein kinase activity that results in an increase in chromosome abnormalities can result in increased susceptibility to cancer. As such, a subject with decreased DNA-dependent protein kinase activity, determined in accordance with the presently disclosed subject matter, is susceptible to, or has an increased "likelihood" of, developing cancer due to an increased potential to develop genetic mutations. See page 15, line 10, through page 16, line 15. Accordingly, applicants respectfully submit that the claims are enabled by the specification in accordance with 35 U.S.C § 112, first paragraph, regarding the ability to determine cancer susceptibility.

Further, applicants respectfully submit that the amended claims are now directed to breast, uterine and head and neck cancer. The specification discloses that lymphoid cells were collected from patients suffering from breast cancer, uterine cancer, and head and neck cancer. See, for example, pages 19 (Example 1) and pages 23-24 (Example 2) of the specification as filed. As such, it is believed that one of ordinary skill in the art, upon review of the present disclosure, could determine the susceptibility to breast, uterine, and head and neck cancers in accordance with the claimed methods. Applicants therefore respectfully submit that present claims 6 and 7 are enabled by the specification in accordance with 35 U.S.C § 112, first paragraph, regarding the type of cancer susceptibility to be determined.

Application Serial No.: 10/559,311

Claim 8 is believed to be enabled as lymphoid cells are explicitly described in Example 1, wherein lymphoid cells were obtained from patients suffering from breast cancer, uterine cancer and head and neck cancer to assess cancer susceptibility by measuring DNA-dependent protein kinase activity. See, for example, pages 19 and 20, of the specification as filed.

As such, applicants respectfully submit that claims 6-8 are enabled by the specification in accordance with 35 U.S.C § 112, first paragraph. Thus, applicants respectfully request that the rejection of claims 6-8 under 35 U.S.C. § 112, first paragraph, be withdrawn, and request that claims 6-8 be allowed at this time.

Response to the Rejection of Claims 6 and 8 Under 35 U.S.C. § 102(b)

Claims 6 and 8 stand rejected under 35 U.S.C. § 102(b) upon the contention that the claims are anticipated by Ogawa et al. Specifically, the Examiner contends that Ogawa et al. teach a method for measuring protein kinase activity in a test sample consisting of the steps of contacting the sample with a substrate peptide phosphorylated by the protein kinase under conditions necessary for the phosphorylation reaction and detecting a change in the phosphorylation level of the substrate peptide. Therefore, the Examiner asserts that because Ogawa et al. teach measuring DNA-dependent protein kinase activity, and the only active step of the claimed methods is measuring protein kinase activity, all the limitations of the rejected claims are met.

The positions of the Examiner as summarized above with respect to the rejected claims are respectfully traversed as described below.

Claim 6 presently recites a method for determining cancer susceptibility by measuring DNA-dependent protein kinase activity in cells derived from a test subject, wherein the cancer is selected from the group consisting of breast cancer, uterine cancer, and head and neck cancer. Claim 6 has been presently amended to recite “wherein the cancer is selected from the group consisting of breast cancer, uterine cancer, and head and neck cancer”. Support for the amendment can be found throughout the specification, including particularly in the specification as originally filed at page 12, lines 11-15; page 19, lines 7-10; and page 24, lines 1-2. Thus, no new matter has been added by the amendment to claim 6.

Applicants respectfully submit that Ogawa et al. fails to teach or suggest a method of determining cancer susceptibility, particularly breast, uterine, and head and neck cancer, by measuring DNA-dependent protein kinase activity. Specifically, Ogawa et al. does not disclose nor suggest the possibility that cancer susceptibility can be determined by measuring DNA-dependent protein kinase activity. In fact, Ogawa et al. does not even mention the word susceptibility. In marked contrast, Ogawa et al. is, at best, generally interested in providing methods of measuring the activity of DNA-dependent protein kinase and other protein kinases. See, for example, page 3, lines 23-25, of Ogawa et al. Accordingly, applicants respectfully submit that describing methods of measuring the activity of various protein kinases is not tantamount to determining cancer susceptibility in a subject by measuring DNA-dependent protein kinase activity. As such, applicants respectfully submit that Ogawa et al. does not anticipate claim 6 as it does not teach each and every element of claim 6. Applicants therefore respectfully request withdrawal of the rejection of

Application Serial No.: 10/559,311

claim 6 under 35 U.S.C. §102(b) as being anticipated by Ogawa et al. Allowance of claim 6 is also respectfully requested.

Since claim 8 depends directly from claim 6 and therefore shares the novel features of claim 6, it too is believed to be patentable over Ogawa et al. for at least the reasons state above. Applicants therefore respectfully request withdrawal of the rejection of claim 8 on the basis of Ogawa et al. Allowance of claim 8 is also respectfully requested.

Response to the Rejection of Claims 6-8 Under 35 U.S.C. § 102(b)

Claims 6-8 stand rejected under 35 U.S.C. § 102(b) upon the contention that the claims are anticipated by Auckley et al. The Examiner contends that Auckley et al. teach DNA-dependent protein kinase activity is reduced in blood samples from lung cancer patients compared to control non-lung cancer patients. Accordingly, the Examiner asserts that since Auckley et al. teach the same method steps as the instant application and the rejected claims do not define the specific cancer susceptibility determined by the method, all the limitations of the claims have been met.

The positions of the Examiner as summarized above with respect to the rejected claims are respectfully traversed as described below.

Claim 6 presently recites a method for determining cancer susceptibility by measuring DNA-dependent protein kinase activity in cells derived from a test subject, wherein the cancer is selected from the group consisting of breast cancer, uterine cancer, and head and neck cancer. Claim 7 presently recites a method for

Application Serial No.: 10/559,311

determining cancer susceptibility, the method comprising the steps of: measuring DNA-dependent protein kinase activity in cells derived from a test subject; measuring DNA-dependent protein kinase activity in cells derived from a healthy subject; and comparing the DNA-dependent protein kinase activity in cells derived from the test subject and the DNA-dependent protein kinase activity in cells derived from the healthy subject, wherein the cancer is selected from the group consisting of breast cancer, uterine cancer, and head and neck cancer. Both claims 6 and 7 have been presently amended to recite "wherein the cancer is selected from the group consisting of breast cancer, uterine cancer, and head and neck cancer". Support for the amendments can be found throughout the specification, including particularly in the specification as originally filed at page 12, lines 11-15; page 19, lines 7-10; and page 24, lines 1-2. Thus, no new matter has been added by the amendment to claims 6 and 7.

Applicants respectfully submit that nowhere does Auckley et al. teach or suggest a method for determining cancer susceptibility by measuring DNA-dependent protein kinase activity in cells derived from a subject, wherein the cancer is selected from the group consisting of breast cancer, uterine cancer, and head and neck cancer. Particularly, Auckley et al. does not teach or suggest a relationship between DNA-dependent protein kinase activity and breast cancer, uterine cancer, and head and neck cancer. In marked contrast, Auckley et al. is generally interested in the DNA-dependent protein kinase activity in blood samples from lung cancer patients. Accordingly, applicants respectfully submit that measuring DNA-dependent protein kinase activity in blood samples from lung cancer patients is not tantamount

Application Serial No.: 10/559,311

to determining a subject's susceptibility to breast cancer, uterine cancer, and head and neck cancer by measuring DNA-dependent protein kinase activity, as presently claimed. As such, applicants respectfully submit that Auckley et al. does not anticipate claims 6 and 7 as it does not teach each and every element of either of claims 6 or 7. Applicants therefore respectfully request withdrawal of the rejection of claims 6 and 7 under 35 U.S.C. §102(b) as being anticipated by Auckley et al. Allowance of claims 6 and 7 is also respectfully requested.

Since claim 8 depends directly from claims 6 or 7 and therefore shares the novel features of claims 6 or 7, it too is believed to be patentable over Auckley et al. for at least the reasons state above. Applicants therefore respectfully request withdrawal of the rejection of claim 8 on the basis of Auckley et al. Allowance of claim 8 is also respectfully requested.

New Claim

New claim 11 recites a method for determining cancer susceptibility, comprising: measuring DNA-dependent protein kinase activity in cells derived from a test subject; and determining cancer susceptibility based upon the measured DNA-dependent protein kinase activity, wherein the cancer is selected from the group consisting of breast cancer, uterine cancer, and head and neck cancer. Support for the new claim can be found throughout the specification as originally filed, including but not limited to page 16, lines 6-12, and page 23, lines 9-13. No new matter is considered to have been added.

The subject matter of claim 11 is not believed to be disclosed in any of the prior art documents of record. Further, claim 11 is believed to be patentably distinguished over the cited art of record for at least the reasons discussed above. Allowance of claim 11 is therefore respectfully requested.